| | L # | Hits | Search Text | Time Stamp |
|---|---|---|---|---|
| 1 | L1 | 668 | 424/178.1,179.1,181.1,182.1.ccls. | 2002/10/16 14:12 |
| 2 | L2 | 109 | maytansinoid or maytansine or maytansinol | 2002/10/16 14:13 |
| 3 | L3 | 3 | 1 and 2 | 2002/10/16 14:16 |
| 4 | L4 | 9389 | spdp or spp | 2002/10/16 14:17 |
| 5 | L5 | 162 | 1 and 4 | 2002/10/16 14:20 |
| 6 | L6 | 1 | 3 and 4 | 2002/10/16 14:22 |
| 7 | L7 | 8122 | spp | 2002/10/16 14:23 |
| 8 | L8 | 6 | 7 and 1 | 2002/10/16 14:26 |
| 9 | L9 | 202 | 424/179.1.ccls. | 2002/10/16 14:26 |
| 10 | L10 | 57819 | disulfide or thioether or peptidase or esterase or (acid adj labile) or photolabile | 2002/10/16 14:28 |
| 11 | L11 | 121 | 9 and 10 | 2002/10/16 14:28 |
| 12 | L12 | 0 | 11 and 3 | 2002/10/16 14:28 |

L14 ANSWER 1 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002100962 EMBASE
TITLE: Inhibitors of protein-protein interactions.
AUTHOR: Ockey D.A.; Gadek T.R.
CORPORATE SOURCE: T.R. Gadek, Genentech, Inc., One DNA Way, South San Francisco, CA 94080, United States. trg@gene.com
SOURCE: Expert Opinion on Therapeutic Patents, (2002) 12/3 (393-400).
Refs: 40
ISSN: 1354-3776 CODEN: EOTPEG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
022 Human Genetics
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Protein-protein interactions are the basis of a number of intra- and extracellular processes. One of the challenges facing the pharmaceutical industry in the post genomic era is the rational identification and inhibition of this class of targets. Examples are presented of currently marketed drugs, compounds in clinical development and lead molecules in research programmes, which have been identified as inhibitors of protein-protein interactions. Modern drug discovery tools, including the use of humanised antibodies to validate targets and protein SARs in the identification of lead molecules, have brought these targets within reach.

L14 ANSWER 2 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002305111 EMBASE
TITLE: vMIA, a viral inhibitor of apoptosis targeting mitochondria.
AUTHOR: Goldmacher V.S.
CORPORATE SOURCE: V.S. Goldmacher, ImmunoGen, Inc., 128 Sidney Street, Cambridge, MA 02139, United States. victor.goldmacher@immunogen.com
SOURCE: Biochimie, (2002) 84/2-3 (177-185).
Refs: 54
ISSN: 0300-9084 CODEN: BICMBE
PUBLISHER IDENT.: S 0300-9084(02)01367-6
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 004 Microbiology
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Human cytomegalovirus encodes a powerful cell death suppressor vMIA (viral mitochondria-localized inhibitor of apoptosis), also known as pUL37x1. vMIA, a product of the immediate early gene UL37 exon 1, is predominantly localized in mitochondria, where it appears to form a complex with adenine nucleotide translocator, believed to be a component of the mitochondrial transition pore complex. vMIA suppresses apoptosis by blocking permeabilization of the mitochondrial outer membrane. Expression of vMIA protects cells against apoptosis triggered by diverse stimuli, including ligation of death receptors, exposure to certain cytotoxic drugs, and infection with an adenovirus mutant deficient in E1B19K. Deletion mutagenesis of vMIA revealed two domains that are necessary and, together, sufficient for its anti-apoptotic activity. The first domain contains a mitochondrial targeting signal. The function of the second domain is still unknown. vMIA does not share any significant amino acid sequence homology with Bcl-2, and, unlike Bcl-2 or Bcl-x(L), it does not bind BAX or VDAC. These structural and functional differences between vMIA and Bcl-2 suggest that vMIA represents a separate class of cell death suppressors. Experiments with vMIA-deficient CMV (human cytomegalovirus) mutants

provide strong evidence that the anti-apoptotic function of vMIA is required to prevent CMV-induced apoptosis, and is necessary for viral replication. In addition to vMIA, UL37 encodes two longer splice-variant proteins, gpUL37 and GP37(M). Biological functions of these proteins have not yet been identified, and may be unrelated to their anti-apoptotic activity. The identification of vMIA and the finding that its anti-apoptotic function is required for CMV replication provides a rationale for the development of anti-CMV pharmaceuticals that would inactivate vMIA and thus restore apoptosis in cells infected with CMV. .COPYRGT. 2002 Societe francaise de biochimie et biologie moleculaire / Editions scientifiques et medicales Elsevier SAS. All rights reserved.

L14 ANSWER 3 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002140767 EMBASE
TITLE: Antibodies for neoplastic disease: Solid Tumors.
AUTHOR: Matthews I.T.W.
CORPORATE SOURCE: I.T.W. Matthews, ChemOrations Ltd., Yammond, North Heath Lane, Horsham, United Kingdom
SOURCE: Applied Biochemistry and Biotechnology - Part B Molecular Biotechnology, (2002) 21/1 (91-97).
Refs: 32
ISSN: 1073-6085 CODEN: MLBOEO
COUNTRY: United States
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L14 ANSWER 4 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002216497 EMBASE
TITLE: Antimitotic peptides and depsipeptides.
AUTHOR: Hamer E.; Covell D.G.
CORPORATE SOURCE: E. Hamel, NCI-Frederick, Div. of Cancer Treatment/Diagnostic, National Institutes of Health, Building 469, Frederick, MD 21702, United States. hamele@mail.nih.gov
SOURCE: Current Medicinal Chemistry - Anti-Cancer Agents, (2002) 2/1 (19-53).
Refs: 233
ISSN: 1568-0118 CODEN: CMCACI
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Tubulin is the target for an ever increasing number of unusual peptides and depsipeptides that were originally isolated from a wide variety of organisms. Since tubulin is the major component of cellular microtubules, which maintain cell shape in interphase and form the mitotic spindle, most of these compounds are highly toxic to mammalian cells. These peptides and depsipeptides disrupt cellular microtubules and prevent formation of a functional spindle, resulting in the accumulation of cultured cells in the G2/M phase of the cell cycle through specific inhibition of mitosis. At the biochemical level, the compounds all inhibit the assembly of tubulin into polymer and, in the cases where it has been studied, strongly suppress microtubule dynamics at low concentrations. In most cases the peptides and depsipeptides inhibit the binding of vinblastine and vincristine to tubulin in a noncompetitive manner, inhibit tubulin-dependent GTP hydrolysis, and interfere with nucleotide turnover at the exchangeable GTP site on .beta.-tubulin. Most of the peptides and depsipeptides induce tubulin to form oligomers of aberrant morphology, including tubulin rings that vary in diameter depending on the (depsi)

peptide under study. The purpose of this review is to give an overview of the cellular, biochemical, in vivo, and SAR aspects of this group of compounds. We also summarize initial efforts by computer modeling to decipher a pharmacophore among the diverse structures of these peptides and depsipeptides.

L14 ANSWER 5 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001087283 EMBASE
TITLE: PSMA specific antibodies and their diagnostic and therapeutic use.
AUTHOR: Holmes E.H.
CORPORATE SOURCE: E.H. Holmes, Northwest Biotherapeutics Inc., Northwest Hospital, Molecular Medicine, 21720 23rd Drive SE, Bothell, WA 98021, United States. eholmes@nwbio.com
SOURCE: Expert Opinion on Investigational Drugs, (2001) 10/3 (511-519).
Refs: 56
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
023 Nuclear Medicine
027 Biophysics, Bioengineering and Medical Instrumentation
028 Urology and Nephrology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Prostate-specific membrane antigen (PSMA) is a membrane-bound glycoprotein highly restricted to prostatic epithelial cells. PSMA expression is increased in association with prostatic ***cancer*** , particularly in hormone refractory disease. Given its membrane-bound character, PSMA is an ideal sentinel molecule for use in targeting prostatic ***cancer*** cells. Monoclonal antibodies specific for PSMA are available, beginning with the antibody 7E11.C5 which originally defined PSMA and which has been developed for use in ***cancer*** detection via immunoscintiscanning in the ProstaScint.RTM. test. Newer second generation antibodies specific for both linear amino acid sequence epitopes and protein conformational epitopes on the extracellular domain of PSMA have been reported. Although most of these are murine antibodies, both humanised and fully human examples have been developed. These antibodies are beginning to work their way into clinical applications for potential improved diagnostic and therapeutic uses. Results to date suggest that antibodies specific for extracellular epitopes are significantly better for clinical uses in vivo than the 7E11.C5 antibody that is specific for an intracellular epitope. Current knowledge relating to PSMA-specific antibodies and their clinical uses and potential is described and evaluated.

L14 ANSWER 6 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001210827 EMBASE
TITLE: Chemotherapy of thymomas and thymic carcinomas.
AUTHOR: Chahinian A.P.
CORPORATE SOURCE: Dr. A.P. Chahinian, Division of Medical Oncology, Department of Medicine, Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, NY 10029, United States
SOURCE: Chest Surgery Clinics of North America, (2001) 11/2 (447-456).
Refs: 55
ISSN: 1052-3359 CODEN: CSCAFT
COUNTRY: United States
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 014 Radiology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
037 Drug Literature Index
LANGUAGE: English

SUMMARY LANGUAGE: English

AB Thymomas are chemosensitive tumors with overall response rates of about 70% to various chemotherapy regimens. A fraction of patients (up to 25%-30%) will obtain a CR after chemotherapy. These results justify the use of chemotherapy in a multimodality fashion for the treatment of patients with advanced tumors. With radiotherapy added to chemotherapy, if necessary and if technically feasible, inoperable tumors may become resectable, leading to excellent long-term survival. On the other hand, thymic carcinomas are more refractory to chemotherapy, and their prognoses remain poor.

L14 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:336175 CAPLUS
DOCUMENT NUMBER: 136:63345
TITLE: Technology evaluation: C242-DM1, ImmunoGen Inc
AUTHOR(S): Smith, Suzanne
CORPORATE SOURCE: Sutherland, NSW 1499, Australia
SOURCE: Current Opinion in Molecular Therapeutics (2001), 3(2), 198-203
CODEN: CUOTFO; ISSN: 1464-8431
PUBLISHER: PharmaPress Ltd.
DOCUMENT TYPE: Journal; ***General Review***
LANGUAGE: English

AB A review. C242-DM1 is a ***tumor*** -activated immunotoxin under development by GlaxoSmithKline plc (formerly SmithKline Beecham plc), under licence from ImmunoGen Inc, as a potential treatment for colon ***tumor*** . It consists of a colon ***cancer*** -specific humanized antibody, C242, conjugated to the ***maytansine*** deriv. DM1. In preclin. studies, C242-DM1 caused complete ***tumor*** regression in animal models of both human pancreatic and non-small cell lung ***cancer*** (NSCLC) at non-toxic doses. C242-DM1 has also been evaluated in an immunoconjugate combination with J-591 (Cornell University). The J591-DM1 immunoconjugate demonstrated effective, antigen-specific delivery of a highly cytotoxic drug to PSMA-pos. Pca cells in vitro and in vivo with low systemic toxicity. Results from studies in monkeys showed that C242-DM1 had no significant toxicity or side effects, when administered at doses higher than those that were previously shown to completely eradicate human colon tumors in mice [271420]. ImmunoGen acquired the right to evaluate, and an option to license, technol. related to maytansines from Takeda. In Feb. 1999, ImmunoGen and SmithKline Beecham signed a US $45 million development and commercialization agreement for C242-DM1 [313493]. In August 1997, Immunogen received an SBIR grant to advance development of huC242-DM1 [258356]. EP-00425235, held by ImmunoGen, covers conjugated forms of ansamitocin ( ***maytansine*** ) derivs. Takeda holds several patents for the prodn. of ansamitocin and its analogs, the first one being JP-53124692.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001434536 EMBASE
TITLE: Targeted drug conjugates: Principles and progress.
AUTHOR: Garnett M.C.
CORPORATE SOURCE: M.C. Garnett, School of Pharmaceutical Sciences, University of Nottingham, University Park, Nottingham NG7 2RD, United Kingdom. martin.garnett@nottingham.ac.uk
SOURCE: Advanced Drug Delivery Reviews, (17 Dec 2001) 53/2 (171-216).
Refs: 224
ISSN: 0169-409X CODEN: ADDREP
PUBLISHER IDENT.: S 0169-409X(01)00227-7
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles

039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Reports of targeting drugs using antibodies have appeared in the literature since 1958, but exciting clinical results in this field have only been reported in the last few years. Progress in this field has occurred largely through an understanding how drug-immunoconjugates work. The objective of this review is to draw together the fundamental principles on which this field of work is based, to examine the evidence supporting those principles, and the effectiveness and selectivity of targeted drug conjugates. The activity of many drug-immunoconjugates can now largely be accounted for by the underlying principles. Excellent development work, both with conventional anti- ***cancer*** agents and very potent drugs have led to a number of interesting clinical trials. In the best Phase I and II trials, good evidence of effectiveness have been reported, which suggest that drug-immunoconjugates may now be heralding a new era for chemotherapy. .COPYRGT. 2001 Elsevier Science B.V. All rights reserved.

L14 ANSWER 9 OF 34 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001087853 MEDLINE
DOCUMENT NUMBER: 20574434 PubMed ID: 11125291
TITLE: [Targeting of antitumor drugs with monoclonal antibodies]. Ciblage de molecules antitumorales par les anticorps monoclonaux.
AUTHOR: Monneret C; Florent J C
CORPORATE SOURCE: Institut Curie, 26, rue d'Ulm, 75248 Paris Cedex 05.
SOURCE: BULLETIN DU CANCER, (2000 Nov) 87 (11) 829-38. Ref: 68
Journal code: 0072416. ISSN: 0007-4551.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
***General Review; (REVIEW)***
(REVIEW, ACADEMIC)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010118
AB About forty years ago, immuno-targeting of antitumor drugs has been addressed as a way to improve their selectivity towards ***tumor*** cells. Despite the wide display of researches to solve inherent problems within this approach, rare were the immuno-conjugates which reached the clinical level. In any case, none of them was introduced in chemotherapy. However, there was a renewal of activity for the last ten years, due, in part, to the access to very highly cytotoxic-containing immuno-conjugates such as those elaborated from maytansinoides, enediynes or intercalating agents CC1065. It was also due to the design of the Adept concept. This antibody-directed enzyme prodrug therapy is based upon the use of monoclonal antibody to target an enzyme at the ***tumor*** cell surface which ultimately is expected to selectively deliver an antitumor drug from a suitable inactive prodrug. In both cases, clinical trials are in progress and one can expect that, at least, some immuno-conjugates will be soon introduced in ***cancer*** chemotherapy.

L14 ANSWER 10 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000424682 EMBASE
TITLE: Anticancer compounds from tissue cultures of medicinal plants.
AUTHOR: Roja G.; Rao P.S.
CORPORATE SOURCE: G. Roja, Heinrich-Heine Univ. Dusseldorf, Institut fur Entwicklungs, Molekular Biologie der Pflanzen, Universitatsstr. 1, D-40225 Dusseldorf, Germany
SOURCE: Journal of Herbs, Spices and Medicinal Plants, (2000) 7/2 (71-102).
Refs: 100
ISSN: 1049-6475 CODEN: JHEPEF

COUNTRY: United States
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB This review summarizes the literature concerning the production of certain anticancer compounds from tissue cultures of medicinal plants. The various problems involved and the possible ways to overcome using biotechnological approaches are discussed.

L14 ANSWER 11 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999428470 EMBASE
TITLE: AGA technical review on the epidemiology, diagnosis, and treatment of pancreatic ductal adenocarcinoma.
AUTHOR: Dimagno E.P.; Reber H.A.; Tempero M.A.
CORPORATE SOURCE: Dr. E.P. Dimagno, Clinic. Practice/Practice Eco. Comm., AGA National Office, Membership Department, 7910 Woodmont Avenue, Bethesda, MD 20814, United States
SOURCE: Gastroenterology, (1999) 117/6 (1464-1484).
Refs: 195
ISSN: 0016-5085 CODEN: GASTAB
COUNTRY: United States
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English

L14 ANSWER 12 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998308281 EMBASE
TITLE: Paclitaxel (Taxol.RTM.): A success story with valuable lessons for natural product drug discovery and development.
AUTHOR: Cragg G.M.
CORPORATE SOURCE: G.M. Cragg, Developmental Therapeutics Program, Div. of Cancer Treatm., Diagn./Ctrs., National Cancer Institute, Bethesda, MD 20892, United States
SOURCE: Medicinal Research Reviews, (1998) 18/5 (315-331).
Refs: 35
ISSN: 0198-6325 CODEN: MRREDD
COUNTRY: United States
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The discovery and development of paclitaxel, which covered a time span of some 30 years, has provided some important lessons for those involved in natural product drug discovery and development. These include the adoption of novel screens as they become available, the elucidation of mechanisms of action, and addressing the supply issue at an early stage of development. These issues, as applied to paclitaxel, are illustrated. The development of the NCI human ***cancer*** cell line screen, and its application to mechanistic studies through use of COMPARE analyses, are discussed, as is the production of the marine-derived anticancer agent, bryostatin 1, which provides another illustration of a successful approach to solving a supply issue. The history of the development of paclitaxel also illustrates the importance of multidisciplinary collaboration, and the various mechanisms used by the NCI Developmental Therapeutics Program for promoting such collaboration are presented.

L14 ANSWER 13 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998251500 EMBASE
TITLE: Tubulin as a target for anticancer drugs: Agents which interact with the mitotic spindle.
AUTHOR: Jordan A.; Hadfield J.A.; Lawrence N.J.; McGown A.T.

CORPORATE SOURCE: A.T. McGown, Cancer Research Campaign, Dept. of Drug Development/Imaging, Paterson Institute for Can. Res., Wilmslow Road, Manchester M20 4BX, United Kingdom
SOURCE: Medicinal Research Reviews, (1998) 18/4 (259-296).
Refs: 193
ISSN: 0198-6325 CODEN: MRREDD
COUNTRY: United States
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Tubulin is the biochemical target for several clinically used anticancer drugs, including paclitaxel and the vinca alkaloids vincristine and vinblastine. This review describes both the natural and synthetic agents which are known to interact with tubulin. Syntheses of the more complex agents are referenced and the potential clinical use of the compounds is discussed. This review describes the biochemistry of tubulin, microtubules, and the mitotic spindle. The agents are discussed in relation to the type of binding site on the protein with which they interact. These are the colchicine, vinca alkaloid, rhizoxin/ ***maytansine*** , and tubulin sulfhydryl binding sites. Also included are the agents which either bind at other sites or unknown sites on tubulin. The literature is reviewed up to October 1997.

L14 ANSWER 14 OF 34 MEDLINE
ACCESSION NUMBER: 1998225977 MEDLINE
DOCUMENT NUMBER: 98225977 PubMed ID: 9564789
TITLE: Natural organic compounds that affect to microtubule functions.
AUTHOR: Iwasaki S
CORPORATE SOURCE: Kitasato Institute, Tokyo, Japan.
SOURCE: YAKUGAKU ZASSHI. JOURNAL OF THE PHARMACEUTICAL SOCIETY OF JAPAN, (1998 Apr) 118 (4) 112-26. Ref: 39
Journal code: 0413613. ISSN: 0031-6903.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) ***General Review; (REVIEW)*** (REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980625
Last Updated on STN: 19980625
Entered Medline: 19980616
AB Microtubules (MT), composed of a protein tubulin (TN) alpha,beta-heterodimer with concomitant other proteins, microtubule associated proteins (MAPs and tau), are known to be the main component of spindles in a mitotic apparatus of eucaryotic cells, and are also involved in many other basic and essential cell functions. There are a number of natural and synthetic compounds that interfere with MT function to cause the mitotic arrest of eucaryotic cells. Such antimitotic agents show a broad biological activity, and can be used for medicinal and agrochemical purposes. On the other hand, they are also important as the biochemical tools for understanding the dynamics of MT network. Most of such antimitotic agents, with a few exceptions, bind to beta-TN. Among them, colchicine (CLC), vinblastine (VLB) and taxol have been of major importance in biochemical studies of MT and in studies of their intracellular functions. The former two both inhibit MT assembly but their binding sites on beta-TN are different; CLC-site and VLB-site, and many MT inhibitors bind to either sites. Taxol bind to TN at a site other than CLC-site and VLB-site, and promote MT assembly. We have worked on a variety of antimitotic agents that bind to CLC, VLB or taxol-site, in discoveries, structures, biological actions and/or interactions with TN. In this paper, I summarized the results of our studies on VLB-site ligands; (1) rhizoxin (RZX), isolated as a phytotoxin produced by a plant

pathogenic fungus, and its related compounds, (2) derivatives of ansamitocin P-3 (ASMP3) ( ***maytansinoid*** : MAY), isolated as a cytotoxic metabolite of an Actinomycete, (3) phomopsin A (PMSA), isolated as a mycotoxin produced by a plant parasitic fungus, (4) dolastatin 10 (DLS10), isolated as a cytotoxic metabolite of a see animal, (5) ustiloxins (USL) A-F, isolated as a mycotoxin produced by a plant pathogenic fungus, (6) arenastation A (ARSA), isolated as a cytotoxic metabolite of a sponge, and its synthetic analogs. From our studies on interactions of these VLB-site ligands with TN, we showed that the presence of a distinct RZX/MAY-binding site which only partially overlap with VLB-site, and that PMSA, DLS10, USLs and ARSA bind to the RZX/MAY site. RZX, ASMP3 and ARSA inhibit the growth of a variety of fungi, including Aspergillus nidulans. In order to obtain information as to the drug-TN interaction at the RZX/MAY site, RZX-resistant beta-TN gene mutants were isolated from RZX-sensitive wild-type A. nidulans. In all the beta-TN gene mutants, single amino acid (100th) alteration, asparagine-to-isoleucine, was observed. Sequence displacement experiments confirmed that this alteration conferred resistance to RZX and ASMP3, and also to ARSA. This resistance mechanism was further verified with yeasts Schizosaccharomyces pombe and Saccharomyces serevisiae. All the natural ligands mentioned above show potent cytotoxicity against human and murine ***tumor*** cells, but VLB, PMSA, DLS10 and USLA are inactive to both RZX-sensitive and -resistant fungal strains.

L14 ANSWER 15 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 2
ACCESSION NUMBER: 1998133499 EMBASE
TITLE: Natural organic compounds that affect to microtubule functions.
AUTHOR: Iwasaki S.
CORPORATE SOURCE: S. Iwasaki, Kitasato Institute, 5-9-1 Shirokane, Minato-ku, Tokyo 108-8642, Japan
SOURCE: Yakugaku Zasshi, (1998) 118/4 (111-126).
Refs: 39
ISSN: 0031-6903 CODEN: YKKZAJ
COUNTRY: Japan
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
AB Microtubules (MT), composed of a protein tubulin (TN) .alpha.,.beta.-heterodimer with concomitant other proteins, microtubule associated proteins (MAFs and .tau.), are known to be the main component of spindles in a mitotic apparatus of eucaryotic cells, and are also involved in many other basic and essential cell functions. There are number of natural and synthetic compounds that interfere with MT function to cause the mitotic of eucaryotic cells. Such antimitotic agents show a broad biological activity, and can be used for medicinal and agrochemical purposes. On the other hand, they are also important as the biochemical tools for understanding the dynamics of MT network. Most of such antimitotic agents, with a few exceptions, bind to .beta.- TN. Among them, colchicine (CLC), vinblastine (VLB) and taxol have been of major importance in biochemical studies of MT and in studies of their intracellular functions. The former two both inhibit MT assembly but their binding sites in .beta.-TN are different; CLC-site and VLB-site, and many MT inhibitors bind to either sites. Taxol bind to TN at a site other than CLC- site and VLB-site, and promote MT assembly. We have worked on a variety of antimitotic agents that bind to CLC, VLB or taxol-site, in discoveries, structures, biological action and/or interactions with TN. In this paper, I summarized the results of our studies on VLB-site ligands; (1) rhizoxin (RZX), isolated as a phytotoxin produced by a plant pathogenic fungus, and its related compounds, (2) derivatives of ansamitocin P-3 (ASMP3) (maytasinoid: MAY), isolated as a cytotoxic metabolite of an Actinomycete, (3) phomopsin A (PMSA), isolated as a mytotoxin produced by a plant parasitic fungus, (4) dolastatin 10 (DLS10), isolated as a cytotoxic metabolite of a see animal, (5) ustiloxins (USL) A-F, isolated as a

mytotoxin produced by a plant pathogenic fungus, (6) arenastatin A (ARSA), isolated as a cytotoxic metabolite of a sponge, and its synthetic analogs. From our studies on interactions of these VLB-site ligands with TN, we showed that the presence of a distinct RZX/MAY-binding site which only partially overlap with VLB- site, and that PMSA, DLS10, USLs and ARSA bind to the RZX/MAY site. RZX, ASMP3 and ARSA inhibit the growth of a variety of fungi, including ASpergillus nidulans. In order to obtain information as to the drug-TN interaction at the RZX/MAY site, RZX-resistant .beta.-TN gene mutants were isolated from RZX-sensitive wild-type A. nidulans. In all the .beta.-TN gene mutants, single amino acid (100th) alteration, asparagine-to-isoleucine, was observed. Sequence displacement experiments confirmed that this alteration conferred resistance to RZX and ASMP3, and also to ARSA. This resistance mechanism was further verified with yeasts Schizosaccharomyces pombe and Saccharomyces serevisiae. All the natural ligands mentioned above show potent cytotoxicity against human and murine ***tumor*** cells, but VLB, PMSA, DLS10 and USLA are inactive to both RZX-sensitive and resistant fungal strains.

L14 ANSWER 16 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97250714 EMBASE
DOCUMENT NUMBER: 1997250714
TITLE: Biological therapies for gastrointestinal cancers.
AUTHOR: Weiner L.M.
CORPORATE SOURCE: Dr. L.M. Weiner, Fox Chase Cancer Center, 7701 Burholme Avenue, Philadelphia, PA 19111, United States
SOURCE: Current Opinion in Oncology, (1997) 9/4 (373-379).
Refs: 23
ISSN: 1040-8746 CODEN: CUOOE8
COUNTRY: United States
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Several new agents with promising activity in gastrointestinal malignancies have been identified in the past several years. Despite these advances, most advanced gastrointestinal malignancies cannot be cured by currently available agents or approaches. Accordingly, efforts to develop new treatment strategies continue to have urgent priority. Much interesting work has been done in the past year. The continued evaluation of these new strategies will identify those with the potential to have clinical effects on patients with gastrointestinal cancers.

L14 ANSWER 17 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97318677 EMBASE
DOCUMENT NUMBER: 1997318677
TITLE: Radiation therapy and 5-fluorouracil in pancreatic ***cancer*** .
AUTHOR: Chakravarthy A.; Abrams R.A.
CORPORATE SOURCE: Dr. R.A. Abrams, Johns Hopkins Oncology Center, Division of Radiation Oncology, 600 N. Wolfe St, Baltimore, MD 21287-8922, United States
SOURCE: Seminars in Radiation Oncology, (1997) 7/4 (291-299).
Refs: 42
ISSN: 1053-4296 CODEN: SRONEO
COUNTRY: United States
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 014 Radiology
016 Cancer
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Combination chemotherapy has not been shown to be superior to single-agent 5-fluorouracil (5-FU) in the treatment of metastatic pancreatic

***cancer*** . Initial studies from Duke University suggest a role for radiation in the management of locally unresectable presentations of this disease. In vivo studies showed that 5-FU could act as a radiation sensitizer. This concept was subsequently tested in a randomized trial by the Gastrointestinal ***Tumor*** Study Group (GITSG). In their studies, combined modality therapy using radiation and 5-FU based chemotherapy prolonged survival in both adjuvant and locally unresectable settings and remains as a standard therapeutic option for appropriately selected patients. Variations on this approach designed to potentiate 5-FU efficacy are under active clinical investigation. This review discusses past and current studies involving 5-FU and radiation and examines some newer strategies involving 5-FU as well as other agents currently of interest.

L14 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:123468 CAPLUS
DOCUMENT NUMBER: 126:216487
TITLE: The development of antibody delivery systems to target ***cancer*** with highly potent maytansinoids
AUTHOR(S): Liu, Changnian; Chari, Ravi V. J.
CORPORATE SOURCE: ImmunoGen, Inc., Cambridge, MA, 02139-4239, USA
SOURCE: Expert Opinion on Investigational Drugs (1997), 6(2), 169-172
CODEN: EOIDER; ISSN: 0967-8298
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; ***General Review***
LANGUAGE: English
AB A review with 18 refs. Improving the ***tumor*** selectivity of cytotoxic drugs through conjugation to ***tumor*** -reactive monoclonal antibodies may lead to novel, more potent agents for ***cancer*** therapy. The ***maytansinoid*** drugs are 100- to 1000-fold more cytotoxic in vitro than current clin. anticancer drugs. The authors recently demonstrated that conjugation of ***maytansinoid*** drugs to monoclonal antibodies renders them highly efficacious against cancers of breast and colon in both in vitro and in in vivo ***tumor*** models. Antibody-maytansinoids represent a new generation of immunoconjugates that may yet fulfil the promise of effective ***cancer*** therapy through antibody targeting of cytotoxic agents.

L14 ANSWER 19 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96127608 EMBASE
DOCUMENT NUMBER: 1996127608
TITLE: Chemotherapy of adenocarcinoma of the pancreas.
AUTHOR: Schnall S.F.; Macdonald J.S.
CORPORATE SOURCE: Temple University Cancer Center, Temple University Hospital, 3322 N Broad St,Philadelphia, PA 19140, United States
SOURCE: Seminars in Oncology, (1996) 23/2 (220-228).
ISSN: 0093-7754 CODEN: SOLGAV
COUNTRY: United States
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Adenocarcinoma of the pancreas is the fifth leading cause of ***cancer*** death in the United States. Although surgery and radiation therapy may improve prognosis in patients with localized and resectable tumors, chemotherapy has produced minimal benefit. Patients with unresectable and/or metastatic pancreatic ***cancer*** are most frequently treated with S-fluorouracil-based regimens which have produced little palliation with no improvement in overall survival. Newer treatment modalities including octreotide, biologic response modifiers, and monoclonal antibodies have been explored and have resulted in some minor responses. Other chemotherapeutic agents such as the taxanes (ie,

paclitaxel and docetaxel) have not been fully evaluated. Initial evaluations of paclitaxel and docetaxel have shown less than 20% response rates. Attempts at dose escalation with growth factor support are also being pursued. The most exciting new agent being tested currently in pancreatic cancers is gemcitabine which has produced overall clinical benefits in as many as 25% of cases.

L14 ANSWER 20 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:197377 BIOSIS
DOCUMENT NUMBER: PREV199698753506
TITLE: Antimitotic natural products and their interactions with tubulin.
AUTHOR(S): Hamel, Ernest
CORPORATE SOURCE: Build. 37, Room 5C25, Natl. Inst. Health, Bethesda, MD 20892 USA
SOURCE: Medicinal Research Reviews, (1996) Vol. 16, No. 2, pp. 207-231.
ISSN: 0198-6325.
DOCUMENT TYPE: ***General Review***
LANGUAGE: English

L14 ANSWER 21 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94357917 EMBASE
DOCUMENT NUMBER: 1994357917
TITLE: [Current status of chemotherapy for pancreatic ***cancer*** : Possibilities and limitations].
MOGLICHKEITEN UND GRENZEN DER ZYTOSTATISCHEN CHEMOTHERAPIE BEIM PANKREASKARZINOM.
AUTHOR: Scheithauer W.
CORPORATE SOURCE: Abteilung fur Onkologie, Universitatsklinik Innere Medizin I, Allgemeines Krankenhaus, Wahringer Gurtel 18-20,A-1090 Wien, Austria
SOURCE: Wiener Klinische Wochenschrift, (1994) 106/22 (704-708).
ISSN: 0043-5325 CODEN: WKWOAO
COUNTRY: Austria
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
048 Gastroenterology
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: German; English
AB The investigation of chemotherapy for pancreatic ***cancer*** has been hampered by the fact that most patients present with severe general illness and thus tolerate this form of treatment poorly. Furthermore, because of the relative inaccessibility of the pancreas it has been difficult to monitor objective response rates. In patients with disseminated disease only few drugs have shown antitumour activity and the response rates generally do not exceed 20%. Several combination regimens have been tested. Of those assessed in randomized trials, the median survival has ranged from 2 to 6.5 months, which is not significantly better than with supportive therapy alone. Endocrine treatment measures and certain experimental treatment approaches such as reversal of multidrug resistance, photodynamic therapy and radioimmunotherapy may represent promising fields for future research. Encouraging preliminary results, however, warrant confirmation in controlled clinical trials. In patients with unresectable though localized pancreatic tumours the use of conventional external-beam radiation therapy plus 5-fluorouracil can significantly increase survival. Combined radiochemotherapy also seems to play an important role in the postoperative adjuvant treatment of potentially curative tumours, increasing the long-term results of surgical management.

L14 ANSWER 22 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94352512 EMBASE
DOCUMENT NUMBER: 1994352512
TITLE: Treatment of neuroendocrine tumors.
AUTHOR: Oberg K.

CORPORATE SOURCE: Department of Internal Medicine, University Hospital,S-751 85 Uppsala, Sweden
SOURCE: Cancer Treatment Reviews, (1994) 20/4 (331-355).
ISSN: 0305-7372 CODEN: CTREDJ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 003 Endocrinology
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L14 ANSWER 23 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94248211 EMBASE
DOCUMENT NUMBER: 1994248211
TITLE: Chemoimmunoconjugates for the treatment of ***cancer***
AUTHOR: Pietersz G.A.; Rowland A.; Smyth M.J.; McKenzie I.F.C.
CORPORATE SOURCE: Austin Research Institute, Austin Hospital, Studley Road,Heidelberg, Vic. 3084, Australia
SOURCE: Advances in Immunology, (1994) 56/- (301-387).
ISSN: 0065-2776 CODEN: ADIMAV
COUNTRY: United States
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L14 ANSWER 24 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94183198 EMBASE
DOCUMENT NUMBER: 1994183198
TITLE: Natural products as anticancer agents.
AUTHOR: Sinha S.; Jain S.
CORPORATE SOURCE: Medical Chemistry Division, Central Drug Research Institute,Lucknow 226 001, India
SOURCE: Progress in Drug Research, (1994) 42/- (53-132).
ISSN: 0071-786X CODEN: FAZMAE
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
LANGUAGE: English

L14 ANSWER 25 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94302288 EMBASE
DOCUMENT NUMBER: 1994302288
TITLE: Salvage chemotherapy in recurrent or refractory squamous cell ***cancer*** of the uterine cervix.
AUTHOR: Alberts D.S.; Garcia D.J.
CORPORATE SOURCE: Arizona Cancer Center, 1515 N Campbell Ave,Tucson, AZ 85724, United States
SOURCE: Seminars in Oncology, (1994) 21/4 SUPPL. 7 (37-46).
ISSN: 0093-7754 CODEN: SOLGAV
COUNTRY: United States
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 010 Obstetrics and Gynecology
016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Squamous cell ***cancer*** of the cervix is a relatively drug-resistant ***tumor*** . Therefore, chemotherapy is predominately reserved for cervical ***cancer*** patients with recurrent or refractory disease following surgery and/or radiation therapy or for

patients who present with far advanced, incurable disease. Objective responses to salvage chemotherapy are generally short lived (4 to 6 months) with few patients surviving more than 1 year. Complete clinical remissions primarily occur at extra-pelvic sites (eg, lung, lymph node, and soft tissue metastases). Bulky pelvic ***tumor*** in an area of prior irradiation remains largely refractory to further therapy. At present, no chemotherapy regimen has proven superior to single-agent cisplatin, which is associated with an approximately 30% objective response rate. The most effective nonplatinum agents appear to be doxorubicin, ifosfamide, mitolactol, and vincristine. Multiple studies have documented improved partial response rates with platinum-based multiagent chemotherapy, but no regimen has been associated with an improved survival duration. To improve the poor prognosis of this patient group, identification of new agents with at least equivalent activity to cisplatin is mandatory. The development of new platinum-based regimens using currently available agents is unlikely to substantially improve patient survival, although better palliative therapy may result from this approach.

L14 ANSWER 26 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93120124 EMBASE
DOCUMENT NUMBER: 1993120124
TITLE: Thymomas: Current experience and future directions in therapy.
AUTHOR: Loehrer P.J.
CORPORATE SOURCE: Indiana University Medical Center, Department of Medicine, Section of Hematology/Oncology, 550 North University Boulevard,Indianapolis, IN 46202-5265, United States
SOURCE: Drugs, (1993) 45/4 (477-487).
ISSN: 0012-6667 CODEN: DRUGAY
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L14 ANSWER 27 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93051071 EMBASE
DOCUMENT NUMBER: 1993051071
TITLE: Antimitotic agents: Chemistry and recognition of tubulin molecule.
AUTHOR: Iwasaki S.
CORPORATE SOURCE: Institute of Applied Microbiology, University of Tokyo, 1-1-1 Yayoi,Bunkyo-ku, Tokyo 113, Japan
SOURCE: Medicinal Research Reviews, (1993) 13/2 (183-198).
ISSN: 0198-6325 CODEN: MRREDD
COUNTRY: United States
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 004 Microbiology
016 Cancer
029 Clinical Biochemistry
052 Toxicology
037 Drug Literature Index
030 Pharmacology
LANGUAGE: English

L14 ANSWER 28 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94000043 EMBASE
DOCUMENT NUMBER: 1994000043
TITLE: The role of chemotherapy in invasive thymoma: A review of the literature and considerations for future clinical trials.
AUTHOR: Tomiak E.M.; Evans W.K.
CORPORATE SOURCE: University of Ottawa,Ottawa, Ont., Canada
SOURCE: Critical Reviews in Oncology/Hematology, (1993) 15/2 (113-124).

ISSN: 1040-8428 CODEN: CCRHEC
COUNTRY: Ireland
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
037 Drug Literature Index
LANGUAGE: English

L14 ANSWER 29 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:239000 BIOSIS
DOCUMENT NUMBER: PREV199344112200
TITLE: Thymomas.
AUTHOR(S): Chahinian, A. Philippe
CORPORATE SOURCE: Mt. Sinai Med. Cent., New York, NY USA
SOURCE: Holland, J. F. [Editor]; Freii, E., III [Editor]; Bast, R. C., Jr. [Editor]; Kufe, D. W. [Editor]; Morton, D. L. [Editor]; Weichselbaum, R. R. [Editor]. (1993) pp. 2) 1355-1361. Cancer medicine, Third edition, Vols. 1 and 2. Publisher: Lea and Febiger 200 Chesterfield Parkway, Malvern, Pennsylvania 19355, USA.
ISBN: 0-8121-1422-1.
DOCUMENT TYPE: ***General Review***
LANGUAGE: English

L14 ANSWER 30 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92329958 EMBASE
DOCUMENT NUMBER: 1992329958
TITLE: New drugs in the treatment of metastatic breast ***cancer*** .
AUTHOR: Kolaric K.
CORPORATE SOURCE: Central Inst. for Tumors Allied Dis., Ilica 197,41000 Zagreb, Croatia
SOURCE: Libri Oncologici, (1992) 21/1 (55-62).
ISSN: 0300-8142 CODEN: LBOCB3
COUNTRY: Croatia
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English; Serbo-Croatian

L14 ANSWER 31 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 91272088 EMBASE
DOCUMENT NUMBER: 1991272088
TITLE: Chemotherapy in malignant mesothelioma: A review.
AUTHOR: Krarup-Hansen A.; Hansen H.H.
CORPORATE SOURCE: Department of Oncology, The Finsen Institute, Rigshospitalet,DK-2100 Copenhagen, Denmark
SOURCE: Cancer Chemotherapy and Pharmacology, (1991) 28/5 (319-330).
ISSN: 0344-5704 CODEN: CCPHDZ
COUNTRY: Germany
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
035 Occupational Health and Industrial Medicine
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB This review of malignant mesothelioma focuses on the activity of single-agent and combination chemotherapy, a field in which research has thus far been rather unsystematic and sparse. Available results neither accede to any substantial drug activity nor justify the use of standard therapy. Furthermore, even when pooled most findings do not fulfil the

basic criteria for a phase II trial. Prospective (multicenter) phase II trials are recommended for the identification of new agents that show antineoplastic activity in malignant mesothelioma. The use of computed tomography scans can assist in the prediction of the extent of disease both before and during treatment. ***Tumor*** -biological systems using mice xenografts or cell lines of human mesothelioma should be further developed so as to improve the screening of new agents exhibiting potential antineoplastic activity that is especially directed against mesothelioma.

L14 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:441130 CAPLUS
DOCUMENT NUMBER: 115:41130
TITLE: Natural products in ***cancer*** treatment from bench to the clinic
AUTHOR(S): Fox, Brian W.
CORPORATE SOURCE: Paterson Inst. Cancer Res., Christie Hosp., Withington/Manchester, M20 9BX, UK
SOURCE: Transactions of the Royal Society of Tropical Medicine and Hygiene (1991), 85(1), 22-5
CODEN: TRSTAZ; ISSN: 0035-9203
DOCUMENT TYPE: Journal; ***General Review***
LANGUAGE: English
AB A review with 13 refs. discussing the development of natural products (vincristine, ***maytansine*** , dolastatin) and their uses in ***cancer*** treatment and experiences of ***Cancer*** Research Campaign Clin. Trials Committee in clin. trials.

L14 ANSWER 33 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 89286532 EMBASE
DOCUMENT NUMBER: 1989286532
TITLE: Soft tissue sarcomas.
AUTHOR: Lawrence Jr. W.; Neifeld J.P.
CORPORATE SOURCE: Division of Surgical Oncology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA, United States
SOURCE: Current Problems in Surgery, (1989) 26/11 (818 p.).
ISSN: 0011-3840 CODEN: CPSUA7
COUNTRY: United States
DOCUMENT TYPE: Journal; ***General Review***
FILE SEGMENT: 009 Surgery
016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Soft tissue sarcomas in infants and children differ from those in adults in clinical presentation, histology, and response to therapy. For rhabdomyosarcoma, the most common sarcoma in children, each primary site has special characteristics that affect both treatment programs and survival rates. Some results are so good, from the standpoint of survival data, that studies are now in progress to evaluate means of reducing treatment morbidity. Other ongoing studies focus on improved protocols for metastatic or recurrent rhabdomyosarcoma. Results thus far in the IRS trials have proven the value of cooperative clinical trials in the management of patients with this disease.

L14 ANSWER 34 OF 34 MEDLINE
ACCESSION NUMBER: 88209219 MEDLINE
DOCUMENT NUMBER: 88209219 PubMed ID: 3329524
TITLE: Therapeutic selectivity of vinca alkaloids: a role for guanosine 5'-triphosphate?.
AUTHOR: Houghton P J; Houghton J A; Bowman L C; Hazelton B J
CORPORATE SOURCE: Division of Biochemical & Clinical Pharmacology, St Jude Children's Research Hospital, Memphis, Tennessee 38101.
CONTRACT NUMBER: CA 23099 (NCI)
CA 23944 (NCI)
CA 38933 (NCI)

SOURCE: ANTI-CANCER DRUG DESIGN, (1987 Oct) 2 (2) 165-79. Ref: 34
Journal code: 8603523. ISSN: 0266-9536.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
***General Review; (REVIEW)***
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198806
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880620

AB Tubulin, the protein subunit of microtubules, is considered a target for antimitotic agents such as colchicine, ***maytansine*** and the vinca alkaloids vincristine and vinblastine. Of these agents, only vincristine and vinblastine have been found to have clinical utility for treatment of human neoplastic disease. The basis for therapeutic selectivity was examined in a comprehensive model in which human rhabdomyosarcomas were grown as xenografts in mice. This model has allowed a detailed examination of differences between neoplastic and non-neoplastic tissues with respect to binding, retention and metabolism of vinca alkaloids. Of note is that in ***tumor*** tissue, vincristine is tenaciously bound whereas vinblastine is not. In non-neoplastic tissue, retention of both agents is poor. The mechanisms responsible for differential retention between vinca alkaloids and between neoplastic and non-neoplastic tissues were examined. Results suggest that guanosine 5-triphosphate may be implicated in the formation and stability of vinca-tubulin complexes in tissue cytosols. Two models consistent with the data are proposed, and the significance to therapeutic efficacy is discussed.

=> d his

(FILE 'HOME' ENTERED AT 14:39:41 ON 16 OCT 2002)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 14:39:52 ON 16 OCT 2002
L1 1173 S MAYTANSINOID OR MAYTANSINOL OR MAYTANSINE
L2 23897 S ERBB2 OR HERCEPTIN OR HUMAB4D5## OR 4D5 OR 2C4 OR TRASTUZUMAB
L3 4 S L1 AND L2
L4 4 DUP REM L3 (0 DUPLICATES REMOVED)
L5 71781 S MICROTUBULE
L6 69 S L5 AND L2
L7 50 DUP REM L6 (19 DUPLICATES REMOVED)
L8 0 S GENERAL REVIEW/JT
L9 0 S GENERAL REVIEW/PT
L10 3062674 S GENERAL REVIEW/DT
L11 104 S L1 AND L10
L12 3021230 S CANCER OR TUMOR OR TUMOUR OR MALIGNANCY
L13 36 S L11 AND L12
L14 34 DUP REM L13 (2 DUPLICATES REMOVED)